PUBLIC HEALTH REPORT

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Current Status of Tuberculin Testing

This statement represents policies accepted by the United States Public Health Service, American Thoracic Society, National Tuberculosis and Respiratory Disease Association, the California Conference of Local Health Officers and the California State Department of Public Health.

CURRENTLY THE BEST diagnostic tool for the identification of persons infected with M. tuberculosis is the tuberculin skin test. It should be a part of a routine physical examination and should be included among diagnostic tests for all ill persons.

The test of choice and the accepted test in California is the 5 Tuberculin Unit (0.0001 mg) intradermal tuberculin test using PPD-S (Standard)* which is the most specific antigen for identification of infection with M. tuberculosis. PPD-C (Commercial) may be used when PPD-S is not available. The Tine and Heaf tests are screening tests only, and all doubtful reactions should be confirmed with the accepted intradermal tuberculin test. Disadvantages of these tests are that accurate dosage cannot be controlled or measured, and some tests use OT (Old Tuberculin) which is not as specific as PPD-S or PPD-C for identifying infection with M. tuberculosis. The 5TU test dose was derived after hundreds of thousands of tests which sought to select a single dose which would yield sensitivity in 95 percent of the infected population. Tests with doses of increasing strength not only are not practical but have increasing loss of specificity, *i.e.*, stronger doses than 5TU elicit an increasing number of cross reactions, or "false positives" due to infection with atypical mycobacteria.* Cross reactions occur in minimal numbers with the 5TU dose of PPD, and vary with the prevalence and geographic location of atypical infection in the United States, being more prevalent in warm, dry, low altitude areas. Most cross reactions to the 5TU test dose tend to be small and fall in the 5 to 10 mm size range. By contrast, specific reactions to M. tuberculosis average around 16 mm in size with a range of 12 to 20 mm for 66 percent of the population and 8 to 24 mm for 95 percent of the population. Specific reactions become fewer and fewer with decreasing reaction size. Therefore, we recognize a size range of 5 to 10 mm where specific and cross reaction sizes overlap which we arbitrarily term as "doubtful," meaning we question whether they are caused by true tuberculous infection, or by some cross-reacting atypical mycobacterial infection. The probability of true tuberculous infection increases with increasing reaction size, and the probability of a cross sensitivity increases with decreasing reaction size.

Comparative Mantoux testing has recently been introduced as a method for distinguishing more precisely between specific and cross reactions. In this procedure, two intradermal tests are given simultaneously, one on each forearm, one test with 5TU of PPD-S tuberculin and the other with a corresponding dose of a PPD-B (Battey) prepared from an atypical Group III (Battey) bacillus. Both tests are read after 48 or 72 hours, as in the standard Mantoux test, by measuring the widest transverse diameter of induration. Results are interpreted according to the comparative sizes of the

*The work of Florence Seibert of the Henry Phipps Institute in Philadelphia in making a better tuberculin culminated in 1934 in the development of Purified Protein Derivative (PPD), a highly potent and stable product without sensitizing properties. One batch, prepared by Seibert in 1939-40, was adopted by the World Health Organization in 1952 as the international standard for mammalian type PPD tuberculin and was designated PPD-S. Dosage is measured in terms of protein nitrogen and expressed in milligrams. PPD-S is currently being made available by the United States Public Health Service through local health departments.

*The human tubercle bacillus is but one of a group of mycobacteria that contains species ranging from saprophytes to obligate parasites. As far back as 1930, it was suspected by some workers that not all reactions to tuberculin could be attributed to tuberculous infection, especially those reactions elicited by large doses of tuberculin. These cross reactions were found to be due to mycobacteria other than tubercle bacilli, and are referred to as atypical mycobacteria. Commonly they are classified by Runyon Groups, *i.e.*, Group I, *M. Kansasii* (photochromogens), Group II, Gause (Scotochromogens), Group III, Battey (non-chromogens), and Group IV, Rapid growers. Recently there has been considerable interest in these atypical mycobacteria because it has been found they sometimes cause tuberculous-like disease involving the lungs and lymph nodes.

two reactions.* At the present time, and for most practical purposes, the Public Health Service has made the following recommendations for the interpretation of comparative testing:

1. Where the reaction size to PPD-S is 10 mm or more and PPD-B is any size } positive for tuberculous infection
2. In the doubtful range (5 to 9 mm) where
   - PPD-S is 5 to 9 mm and PPD-B is larger than S } not tuberculous infection
   - PPD-B is smaller than S } positive for tuberculous infection
   - PPD-B is the same size as S } doubtfully positive for tuberculous infection
3. When PPD-S is less than 5 mm and PPD-S is any size } not tuberculous infection

The identification of persons who are truly infected with M. tuberculosis as distinguished from those who are infected with atypical mycobacteria assumes tremendous importance in light of the United States Public Health Service and Navy studies where 625,000 Navy recruits were dually tested with PPD-S and PPD-B (Battey) antigens. Results of this study* revealed that the risk of developing active diseases is directly related to infection with M. tuberculosis. Data from this paper, "Identifying the Tuberculous Infected,"† by Palmer and Edwards, graphically demonstrates the risk of development of active disease. In those where reaction size is over 12 mm to PPD-S, the risk of developing active disease is 330 per 100,000 men tested. In those with reactions of 6 to 11 mm to PPD-S where the reaction size to PPD-S is greater than to PPD-B the risk is 298 per 100,000 men tested, stressing the importance of not only identifying positive reactors but also of selecting out those among doubtful reactors who are truly infected with M. tuberculosis rather than the atypical mycobacteria. These persons can then receive INH (isoniazid) preventive treatment for one year. The United States Public Health Service chemoprophylaxis field trials over the past 15 years have shown that preventive treatment for one year reduces the risk of development of active disease by 85 percent in the first year after receiving isoniazid.

Groups which should be tuberculin tested are:*

1. All children between 6 and 12 months of age, whether seen in physicians' offices or child health conferences. When feasible, tuberculin testing should be done before measles immunization and smallpox vaccination; this is not possible in mass immunization programs.
2. Annual tuberculin testing on non-reactors in high risk groups up to the age of 4 years and every two years thereafter, depending upon the risk of exposure and the prevalence of tuberculosis in the population group.
3. Persons receiving a medical workup in the differential diagnosis of any disease.
4. Prior to initiating long-term steroid therapy (longer than a few days) and at three-month intervals, for as long as the patient is on steroids.
5. Three months following infection with measles and whooping cough and again in six months in cases where the status of the tuberculin test was not known prior to infection.
6. School populations — tuberculin testing in order of priority:
   (a) School enterers; *i.e.*, kindergarten and first grade students, and students new to school in all grades
   (b) Fourteen-year-olds (age of puberty)
   (c) Other age levels should be included if the school population is composed of large numbers of high-risk individuals, *i.e.*, poverty and minority groups, farm workers, etc.
7. Other high-risk individuals include positive reactors who are also diabetics, silicotics, pregnant women; persons with gastrectomies, Hodgkins or other reticuloendothelial disease.

It is important to stress again that the frequency with which tuberculin tests should be repeated in pediatric age groups should be related to the inci-

*A large reaction to PPD-B does not necessarily signify infection with Battey, as other atypical mycobacterial infections give cross-reactions to Group III (Battey), Group II Gause (Scotochromogens) and avian tuberculous infections and a lesser degree of cross-sensitivity with Group I (*M. Kansasii*) infection. PPD-B is thus useful as a "broad spectrum" antigen for detecting atypical mycobacterial infection, although the reaction cannot be interpreted as specific or diagnostic for one particular type of atypical infection.

†*Identifying the Tuberculous Infected,* JAMA, Vol. 205, No. 3, July, 1968.

*Joint Committee Statement, Academy of Pediatrics and American College of Chest Physicians, 1 Jan. 1966.

dence and prevalence of tuberculous infection in the population and the risk of exposure to communicable tuberculosis.

We have the following information from the United States Public Health Service for school tuberculin testing programs comparing the United States and California for 1967-68 as follows:

United States	*Number Tested*	*Percent Positive Reactors (10 + mm)*
Kindergarten	52,827	0.3%
1st Grade	84,866	0.6%
7th, 8th & 9th Grades	127,708	2.1%

California	*Number Tested*	*Percent Positive Reactors (10 + mm)*
Kindergarten	26,311	0.4%
1st Grade	4,102	0.4%
7th, 8th & 9th Grades	11,606	3.0%

With a positive reactor rate of only 0.4 percent among school enterers in California, it becomes apparent that we are approaching a tuberculin negative population of school enterers. Our goal is a tuberculin negative population of 14-year-olds. Finding a positive reactor among school enterers implies that it should be possible to find the source case since most children of this age have an average of only four close contacts.

X-RAY STUDIES IN ESOPHAGEAL DISEASE

"The esophagus is sort of a buried organ. You can't auscultate it; you can't palpate it, and you can't percuss it. So you really must rely very heavily on the radiologist....

"The barium swallow and cineradiography are standard procedures in most hospitals . . .; and in most cases they will outline the abnormality. But if they don't, several other tests can be utilized in any radiology department.

"The first is the water reflux test. Many patients have esophagitis, and a hiatal hernia may be difficult to demonstrate. We have been able to demonstrate reflux by the use of this test. Usually the radiologist will have the patient fill his stomach with barium and then swallow a glass of water. . . . This allows him a double-contrast procedure. With this double contrast, reflux is usually demonstrated brilliantly.

"The so-called marshmallow test . . . is very helpful. Most people who have dysphagia do not have difficulty swallowing liquids; they have difficulty swallowing solids. The radiologist may miss an abnormality if the patient merely swallows liquid barium. A marshmallow dipped in barium is very helpful in outlining the abnormality. This test can be done by any radiologist, cineradiography later demonstrating the dynamic abnormality to the clinician who can then study it. Not only does this test allow one to find the abnormality; but in most cases, it will reproduce pain when the esophagus is distended; and this makes the patient more aware of the abnormality....

"Finally there is the so-called acid barium mixture. I pointed out that acid in the esophagus in the individual with esophagitis may produce heartburn or reduplication of symptoms. By dropping the pH of barium with some hydrochloric acid, one may find a motor disturbance in the lower esophagus and actually a reduplication of symptoms when the acid barium mixture is taken."

—LAWRENCE D. WRUBLE, M.D., Memphis

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